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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/670,009	09/24/2003	Daniel J. Cosgrove	P04666US08	4403

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MCKEE, VOORHEES & SEASE, P.L.C.
ATTN: PENNSYLVANIA STATE UNIVERSITY
801 GRAND AVENUE, SUITE 3200
DES MOINES, IA 50309-2721

EXAMINER	
SAIDHA, TEKCHAND	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 02/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/670,009	COSGROVE ET AL.	
	Examiner	Art Unit	
	Tekchand Saidha	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *5-7,9-11 and 13-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,8 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/24/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' Amendment and response filed January 31, 2006 is acknowledged. Claims 1-17 are present in this application.

2. ***Election***

Applicant's election of Group I, claims 1-4, 8 & 12, drawn to polynucleotide of SEQ ID NO: 1 encoding a protein having expansin activity with traverse is acknowledged. Applicants request rejoinder of Group I with Group II (drawn to a method of identifying a nucleic acid encoding expansin by hybridization). The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. Process claims that depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with

an allowed product claim will not be rejoined. See " Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

4. Claims 5-7, 9-11 & 13-17 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed.

5. Claims 1-4, 8 & 12 are under consideration in this examination.

6. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

7. The instant specification, page 1, line 6, the current status of U.S. Application Serial No. 09/896, 301, filed June 29, 2001, must be updated, i.e., now abandoned.

8. Claims 8 & 12 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claims 8 & 12 depend from non-elected claims 5 & 11 respectively. Amending the claims as per the suggestions in the preceding lines is required.

9. Claims 8 & 12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 8 & 12 are directed to a nucleotide sequence which encodes a protein with expansin activity, wherein the said sequence is identified by the method using oligonucleotide probe of 4-30 contiguous nucleotides derived from SEQ ID NO: 1' (claim 8), or wherein the said sequence is identified by the method using oligonucleotide primers to amplify expansin encoding based upon SEQ ID NO: 7 (claim 12), The specification discloses a single cucumber cDNA sequence (SEQ ID NO: 1) encoding cucumber cEx-29 expansin protein as the only genus.

The work of Shcherban et. al, PNAS (1995, Sep 26), 92 (20) : 9245-9, cited in **IDS**, **not prior art**, have identified 4 distinct expansins cDNA in rice and at least 6 in Arabidopsis and show that the expansins from among these plant species, are highly conserved in size and sequence similarity (60-87% amino acid sequence identity). Sequence homology of expansin from Strawberry (AC: W81347), for example, and Applicants' amino acid sequence from Arabidopsis expansin (SEQ ID NO. 5) show a sequence homology of about 48.9%; and a nucleotide sequence homology of 25% between Applicants' SEQ ID NO: 1 (cucumber expansin cDNA, AC: T13320) and the nucleotide sequence of strawberry expansin (AC: V68447). Such a low nucleotide sequence homology is insufficient guidance and/or description to prepare or design specific probe(s) or

primer(s) which may be 4-30 nucleotides in length using SEQ ID NO: 1, or design a primer using SEQ ID NO: 7 which is an amino acid sequence (not a DNA), with no description of the hybridization conditions to work with. Further, as discussed above each plant species possess several expansins, a multigene family, where each gene encodes a specific expansin of a given molecular size, not all of these sequences are highly conserved among diverse plants species as discussed above.

The method steps are unclear and remains undescribed. No specific cDNA-fragment(s) or probes or primers, or hybridization conditions are described. No representative number of species corresponding to specific probes or primers of polynucleotides of SEQ ID NO: 1, useful in identifying nucleic acid sequences encoding expansin from other species and/or structure activity relationships are disclosed.

A 'representative number of species' requires that the species which are expressly described be representative of the entire genus. Thus, when there is substantial variation within the genus, it may require a description of the various species which reflect the variation within the genus. In the instant case, the specification fails to describe even a single 'cDNA fragment' or 'primer' of SEQ ID NO : 1 which are 4-30 nucleotides in length by structural and/or physical and chemical characteristics, representative of the entire genus. What constitutes a 'representative number' is an inverse function of the predictability of the art. In such a case, where the members of the genus being claimed are expected to vary widely in their identifying characteristics, such as structure and activity and conditions necessary for the function of the method, written description for each member (probe or primer) and conditions for the assay within the genus will be necessary. Applicants have failed to sufficiently describe the claimed

invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

10. Claims 2-3, 8 & 12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for: 'A polynucleotide sequence encoding an expansin protein wherein the polynucleotide sequence hybridizes under high stringency conditions (6X SSC, 50% formamide ……65°C for 15 min) to the sequence of SEQ ID NO: 1 or a method for identifying a nucleic acid sequence which encodes a protein with expansin activity, comprising the steps of isolating the nucleic acid sequence from a cDNA library by hybridization (under defined stringency conditions) using a DNA probe comprising the sequence of SEQ ID NO : 1', does not reasonably provide enablement for a polynucleotide that is at least 90% identical to the sequence of SEQ ID NO: 1 (claim 2) or a polynucleotide that encodes a polypeptide having at least 90% sequence identity to the sequences of SEQ ID Nos. 2-7 (claim 3); or method of identifying a nucleic acid comprising 'a oligonucleotide probe of 4-30 contiguous bases of SEQ ID NO : 1 (claim 8), or by using a undefined primer of clam 12.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988))[*Ex parte* Forman [230 USPQ 546 (Bd. Pat. App. & Int. 1986)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim. The factors most relevant to this rejection are the scope of the claims, unpredictability in the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

The claim is drawn to encompass 'polynucleotide molecules' or method of identifying a polynucleotide encoding expansin using 'an oligonucleotide of any size ' ..of SEQ ID NO : 1 or fragment of undefined size for a 'PCR primer' or a 'hybridization probe' or obtaining cDNA of varying homology and which encodes amino acid sequences of SEQ ID NO : 2-6 of varying homology (90%) or designing a primer based upon the amino acid sequence of SEQ ID NO : 7. The specification, however, only discloses a single polynucleotide encoding a cucumber cEx-29. In addition the specification teaches the amino acid sequences (SEQ ID Nos. 2-7) of expansins from rice and *Arabidopsis*. Expansins are a new class of proteins that have been identified to be involved in cell wall expansion. Recent studies [Shcherban et. al, PNAS (1995, Sep 26), 92 (20) : 9245-9, not prior art] have identified 4 distinct expansins cDNA in rice and at least 6 in Arabidopsis and show that the expansins from among these plant species, are highly conserved in size and sequence similarity (60-87 % amino acid sequence identity). Searching for sequence homology and comparison of amino acid sequence homology of expansin from Strawberry (AC : W81347), for example, and Applicants' amino acid sequence from Arabidopsis expansin (SEQ ID NO. 5) show a sequence homology of about 48.9%; and a nucleotide sequence homology of 25% between Applicants' SEQ ID NO : 1 (cucumber expansin cDNA, AC : T13320) and the nucleotide sequence of strawberry expansin (AC : V68447). Such a low nucleotide sequence homology is insufficient to use the Applicants' SEQ ID NO: 1 as a probe (much less for a sequence that is 4-30 nucleotides in length or 90% similar to SEQ ID NO: 1 or a DNA that encodes sequences that are 90% similar to the amino acid sequences of SEQ ID Nos. 2-7). in order to clone the expansin polynucleotide from strawberry, even under high stringency conditions. So, if one skilled in the art

were to use a fragment of SEQ ID NO: 1 as probe in order to clone similar genes, based upon the homology factor discussed above, the chances of successful hybridization are extremely low, in view of the unpredictable nature of the art, as well as inadequate guidance provided in the specification.

With regard to method claims 8 & 12 (depends upon non-elected claims 5 & 11 respectively) nucleic acid hybridization or amplification assays are extremely sensitive to the conditions in which they are performed. The buffer composition, pH, temperature, length of time, salt concentrations, quality and source of template nucleic acid, are all variables which determine the reproducibility of a given hybridization experiment. Given the unpredictability of the art and the nature of hybridization experiments in general, it is not sufficient to merely cite hybridization without a clear and explicit recitation of the conditions associated with the hybridization. For example, the definition of stringency as it pertains to hybridization conditions is subject to interpretation and is different from laboratory to laboratory. Therefore, without a clear and explicit recitation of the conditions which were actually used by Applicants in isolating the claimed polynucleotides which hybridize to the disclosed sequences, the skilled artisan would not be able to practice the claimed invention and would not be reasonably apprised of the metes and bounds of the claimed invention. Without such guidance, the experimentation left to those skilled in the art is undue.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims 2 & 3 reciting 90% sequence identity, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired

activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications of any expansin with 90% identity to the enzymes of SEQ ID NOS: 2-7, or the encoding DNA, because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting expansin activity; (B) the general tolerance of expansin to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any expansin residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including DNA encoding expansin with an enormous number of amino acid modifications of the of SEQ ID NOS: 2-7. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of expansin having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue in using the modified enzyme or DNA in the method claimed. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

11. ***Claim Rejections - 35 USC § 112*** (second paragraph)

Claims 3, 8 & 12 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3, line 2 recites ' retains similar biological activity' . The claim is indefinite because it is not clear what similar activities are encompassed by the phrase biological activity. Expansin activity (or cell wall extension activity) is the only known activity described. Substituting ' retains similar biological activity' with ' retains expansin activity' will overcome this rejection.

Claim 8 depends on claim 5, and claim 5 recites '4-30 contiguous bases derived from SEQ ID NO: 1'. The claim is indefinite because it is not clear what derived from mean - as no derivations of SEQ ID NO: 1 are disclosed. Substituting 'derived' with 'obtained' will overcome this rejection.

Claim 12 depends on claim 11, and claim 11 recites 'designing a primer ···based upon SEQ ID NO: 7'. The sequence of SEQ ID NO: 7 is an amino acid sequence. The claim is indefinite because it is not clear how a primer which is a short, single-stranded RNA or DNA segment that functions as the starting point for polymerization of nucleotides, is obtained from a polypeptide sequence of SEQ ID NO: 7, unless translated.

12. **35 U.S.C. § 101**

35 U.S.C. § 101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claims 3-4, 8 & 12 are rejected under 35 U.S.C. § 101 because the claimed invention is directed toward non-statutory subject matter.

In the absence of the hand of man, naturally occurring proteins and/or nucleic acids are considered non-statutory subject matter. *Diamond v. Chakrabarty*, 206 USPQ 193 (1980). This rejection may be overcome by amending the claims 3-4, 8 & 12 to recite wording such as "An isolated polynucleotide or DNA or nucleic acid sequence".

13. ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

(a) Claims 1-4, 8 & 12 rejected under the judicially created doctrine of double patenting over claims 1-3 of U. S. Patent No. 6,255,466 since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

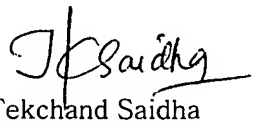
The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: The patented claims 1-3 are species claims drawn to an isolated polynucleotide comprising a nucleotide

sequence of SEQ ID NO: 1 (or a polynucleotide that 90% identical to SEQ ID NO: 1) and which encodes a protein having expansin activity; or a polynucleotide encoding any of the polypeptide of SEQ ID Nos. 2-7 and having expansin activity. The instant claims 1-4, 8 & 12 are genus claims drawn to isolated polynucleotide comprising a nucleotide sequence of SEQ ID NO: 1 (or a polynucleotide that 90% identical to SEQ ID NO: 1) and which encodes a protein having expansin activity or biological activity, or are identified using primers or probes. Claims 1-4, 8 & 12 are broader than the patented claims 1-3. Claim 1-4, 8 & 12 include a genus of variant or diverse sequences as compared to narrower patented species claims. Since species anticipates genus, claims 1-4, 8 & 12 are anticipated by patented claims.

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha whose telephone number is (571) 272 0940. The examiner can normally be reached on 8.30 am - 5.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner' s supervisor, Ponnathapu Achutamurthy can be reached on (571) 272 0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Tekchand Saidha
Primary Examiner, Art Unit 1652
Recombinant Enzymes, E03A61 Remsen Bld.
400 Dulany Street, Alexandria, VA 22314
Telephone : (571) 272-0940

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